

5,15-Dialkyl-Substituted Tetrabenzoporphyrins and Their Zinc Complexes. Synthesis and Spectral Properties

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Abstract—Reactions of phthalimide with capric and stearic acids gave 1-[1-(1-oxo-1*H*-isoindol-3-yl)nonylidene]-2,3-dihydro-1*H*-isoindol-3-one and 1-[1-(1-oxo-1*H*-isoindol-3-yl)heptadecylidene]-2,3-dihydro-1*H*-isoindol-3-one, respectively. The latter were heated with zinc(II) acetate to obtain zinc complexes of 5,15-dioctyl- and 5,15-dihexadecyltetrabenzoporphyrins. The same complexes were synthesized by reaction of 1-(1-oxo-1*H*-isoindol-3-ylmethylidene)-2,3-dihydro-1*H*-isoindol-3-one with capric or stearic acid in the presence of zinc(II) oxide. The corresponding free porphyrin ligands were obtained by treatment of the metal complexes with sulfuric acid.

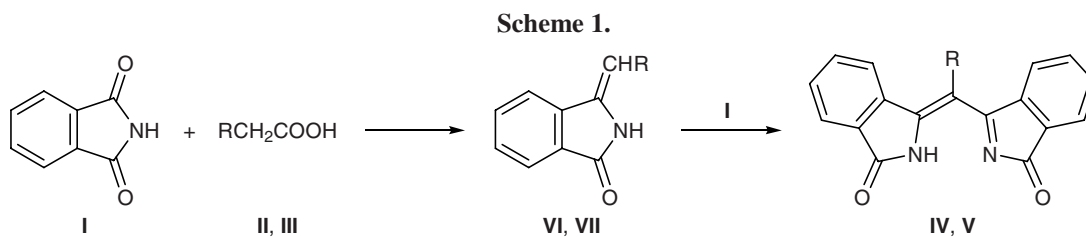
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meso-Substituted tetrabenzoporphyrins constitute one of the most important groups of synthetic analogs of natural porphyrins. Among other factors, interest in these compounds is determined by their improved solubility in a number of organic solvents, which makes it possible to use chromatographic methods for their purification and considerably facilitates applied studies. Up to now, *meso*-aryl-substituted tetrabenzoporphyrins have been explored most thoroughly. They were proposed as dyes [1], photochromic light filters [2], and materials for photodynamic therapy of cancer [3, 4] and nonlinear optics [5]. On the other hand, publications on the synthesis of *meso*-alkyl-substituted tetrabenzoporphyrins are very few in number, though such compounds could attract interest from both theoretical and practical viewpoints.

First representatives of *meso*-tetraalkyl-substituted tetrabenzoporphyrins were synthesized in 1984 [6] by reaction of 3-alkylidenephthalimidines with zinc ace-

tate in the presence of an organic base (tribenzylamine) under helium at 340°C. In this way, *meso*-tetramethyl-, *meso*-tetraethyl-, and *meso*-tetrapropyltetrabenzoporphyrin zinc complexes were obtained. However, the proposed procedure requires preliminary multistep preparation of the corresponding 3-alkylidenephthalimidines, and the presence of four alkyl groups with a carbon chain no longer than three atoms only slightly improves the solubility of porphyrins in organic solvents.

Taking the above into account, we tried to synthesize readily soluble *meso*-tetraalkyl-substituted tetrabenzoporphyrins by reactions of phthalimide (I) with capric and stearic acids II and III in the presence of zinc(II) oxide and sodium hydroxide. The reactions were carried out at 320°C (1 h) under argon. However, no appreciable amounts of the target metal complexes were formed under these conditions, while the products were 1-[1-(1-oxo-1*H*-isoindol-3-yl)nonylidene]-



II, IV, VI, R = C₈H₁₇; III, V, VII, R = C₁₆H₃₃.

2,3-dihydro-1*H*-isoindol-3-one (**IV**) and 1-[1-(1-oxo-1*H*-isoindol-3-yl)heptadecylidene]-2,3-dihydro-1*H*-isoindol-3-one (**V**). Presumably, closure of porphyrin macroring is hampered for steric reasons: neither prolonged reaction nor elevated temperature (380°C) resulted in the formation of the desired complexes, but the amount of tars strongly increased. The reaction of imide **I** with carboxylic acids **II** and **III** is illustrated by Scheme 1. Obviously, compounds **IV** and **V** are formed by condensation of intermediate 3-alkylidene-phthalimidines **VI** and **VII** with initial imide **I**. Compounds **IV** and **V** were isolated and purified by column chromatography on aluminum oxide. In addition, from the reaction mixtures we isolated small amounts of phthalimidines **VI** and **VII** as light yellow waxy substances which showed in the mass spectra peaks from the molecular ions with m/z 257 and 369, respectively. Compounds **IV** and **V** are dark red substances which are readily soluble in various organic solvents. Their structure was confirmed by the analytical data and electronic absorption, ^1H NMR, and mass spectra.

Introduction of an octyl or hexadecyl substituent into the molecule of 1-[1-(1-oxo-1*H*-isoindol-3-ylmethylidene)-2,3-dihydro-1*H*-isoindol-3-one (**VIII**) [7] leads to considerable changes in the electronic absorption spectrum. The spectrum of **VIII** contains three absorption bands in the visible region, while compound **IV** displays only two less resolved bands (Fig. 1). These findings suggest strong association of molecules **IV** in solution. In addition, the absorption maxima are displaced by 45–47 nm to shorter wavelengths, presumably due to distortion of planar structure of molecule **IV** having a bulky alkyl substituent. On the other hand, the electronic absorption spectra of

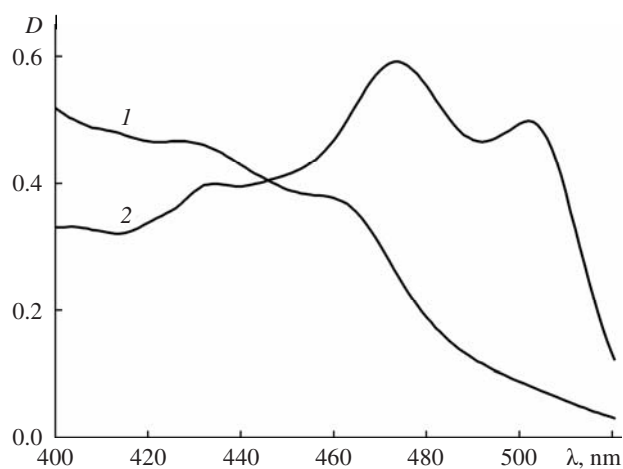


Fig. 1. Electronic absorption spectra of (1) compound **IV** in carbon tetrachloride and (2) compound **VIII** in acetone.

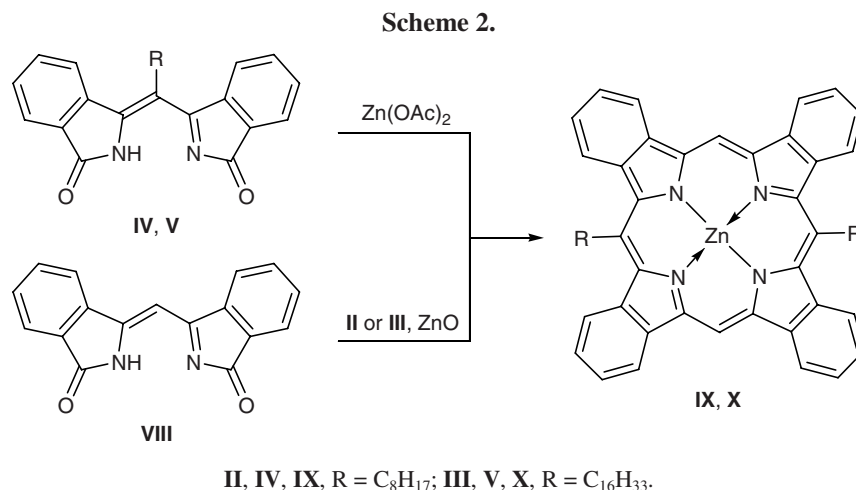
compounds **IV** and **V** are almost similar (see Experimental), i.e., extension of the alkyl chain from 8 to 16 carbon atoms almost does not affect the absorption pattern.

In the ^1H NMR spectrum of **IV**, the most downfield signal is a broadened singlet at δ 10.99 ppm, which belongs to the NH proton. Eight protons in the benzene rings of two isoindole fragments resonate as a multiplet at δ 7.84–7.22 ppm. The upfield region of the spectrum contains signals from protons in the alkyl substituent. Two protons of the α -methylene group give rise to a triplet at δ 2.26 ppm, a broadened singlet at δ 1.25 ppm belongs to 12 internal methylene protons, and signal from the terminal methyl group appeared as a triplet at δ 0.86 ppm. The ^1H NMR spectrum of **V** is qualitatively similar to the spectrum of **IV**, the only difference being the signal intensity ratio.

The mass spectrum (electron impact) of **IV** contained the molecular ion peak with m/z 386 (I_{rel} 25%), as well as peaks from fragment ions with m/z 371 (35%) [$M - \text{CH}_3$] $^+$ and 287 (33%) [$M - \text{C}_7\text{H}_{15}$] $^+$. The base peak in the spectrum, m/z 120, corresponds to the isoindole fragment. In the mass spectrum of **V** we observed the following ion peaks, m/z : 498 (I_{rel} 29%) [M] $^+$, 368, 331, 274, and others.

By heating compounds **IV** and **V** with excess zinc(II) acetate at 320°C for 30 min we obtained (5,15-dioctyltetrabenzoporphyrinato)zinc(II) (**IX**) and (5,15-dihexadecyltetrabenzoporphyrinato)zinc(II) (**X**), respectively. The same complexes were synthesized in another way, by reaction of 1-(1-oxo-1*H*-isoindol-3-ylmethylidene)-2,3-dihydro-1*H*-isoindol-3-one (**VIII**) [7] with acid **II** or **III** in the presence of zinc(II) oxide, the reaction temperature and time being the same (Scheme 2). Complexes **IX** and **X** were isolated from the reaction mixture and purified by chromatography on aluminum oxide using carbon tetrachloride–dioxane (2:1 by volume) as eluent. The free ligands, 5,15-dioctyltetrabenzoporphyrine (**XI**) and 5,15-dihexadecyltetrabenzoporphyrine (**XII**), were obtained by dissolution of complexes **IX** and **X** in 100% sulfuric acid; the solution was held for 2 h at 20°C and diluted with water. Porphyrins **XI** and **XII** were purified by column chromatography.

Compounds **IX–XII** are green substances that are readily soluble in a number of organic solvents. Their purity was checked by TLC, and the structure was confirmed by elemental analysis and ^1H NMR and electronic absorption spectroscopy. The ^1H NMR spectrum of complex **IX** contained a downfield singlet at



δ 11.03 ppm from two *meso*-protons, a multiplet at δ 7.75–7.36 ppm from 16 protons in the isoindole fragments, a triplet at δ 2.77 ppm from four protons in the α -methylene groups of two alkyl substituents, a singlet at δ 1.36 ppm from 24 protons of the other methylene groups, and a triplet at δ 0.82 ppm from six protons of the terminal methyl groups in the alkyl substituents. The ^1H NMR spectra of ligands **XI** and **XII** resemble those of the corresponding zinc complexes **IX** and **X**; the difference is that the ligands display a singlet in a very strong field, at δ –2.41 and –2.35 ppm for **XI** and **XII**, respectively, which belongs to intracyclic NH protons.

The electronic absorption spectra of zinc complexes **IX** and **X** and ligands **XI** and **XII** (Fig. 2; see Experimental) are very similar with the spectra of tetra-benzoporphyrin and its zinc(II) complex [8]. Two main absorption bands (*Q* and Soret) are present in the visible region, and their position does not depend on the length of the *meso*-alkyl substituent. The Soret band in the spectra of complexes **IX** and **X** has its maximum at λ 427 nm, and the *Q*-band, at λ 626 nm. Metal-free compounds **XI** and **XII** are characterized by a small bathochromic shift of the absorption maxima (by 5–6 nm) relative to the corresponding maxima of tetra-benzoporphyrin. Thus introduction of two long-chain alkyl groups into the two opposite *meso*-positions of tetra-benzoporphyrin and its zinc complex almost does not affect the electronic absorption spectra. Obviously, alkyl groups, in contrast to phenyl [7, 9, 10], induce no distortion of the planar structure of the porphyrin macroring. According to the results of AM1 quantum-chemical calculations of molecule **XI**, the saddle-like distortion of the macroring is insignificant, and the isoindole fragments deviate from the macroring plane

by an angle of no more than 12° . In addition, the planar structure of porphyrin molecules **XI** and **XII** follows from the position of the NH signals in the ^1H NMR spectra (see above); these signals are displaced only slightly downfield relative to the NH signal of tetra-benzoporphyrin (δ –2.53 ppm) [11] whose molecule is planar. It is known that strong deviations from planar structure induced by introduction of phenyl substituents into the *meso*-positions of tetra-benzoporphyrin lead to a considerable downfield shift of the NH protons [7, 10].

Thus we have synthesized in two ways tetra-benzoporphyrin derivatives with two long-chain alkyl substituents in the opposite *meso*-positions, which possess improved solubility in organic solvents. As follows from analysis of their spectral parameters and quantum-chemical calculations, molecules of the obtained compounds have planar structure.

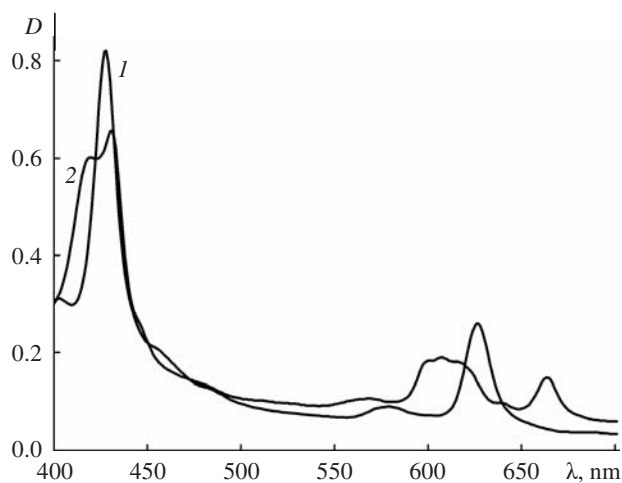


Fig. 2. Electronic absorption spectra of compounds (1) **IX** and (2) **XI** in carbon tetrachloride.

EXPERIMENTAL

The electronic absorption spectra were measured on a Hitachi UV-2000 spectrophotometer. The ^1H NMR spectra were recorded from solutions in CDCl_3 relative to tetramethylsilane (internal reference) on a Bruker AMD-200 instrument. The mass spectra were obtained on a Varian Saturn 2000R GC-MS system. The elemental compositions were determined using a FlashEA 1112 CHNS-O Analyzer.

Reaction of phthalimide with carboxylic acids in the presence of zinc(II) oxide (general procedure). A mixture of 0.01 mol of phthalimide (**I**), 0.02 mol of acid **II** or **III**, 0.5 g of zinc(II) oxide, and 0.2 g of sodium hydroxide was heated for 1 h at 320°C in a stream of argon. The mixture was cooled, excess acid **II** or **III** was removed by washing the mixture in succession with a 10% solution of potassium hydroxide and water. The residue was dissolved in 30 ml of chloroform, the solution was treated with 20 ml of 20% hydrochloric acid, the organic phase was separated, the solvent was removed, the residue was dissolved in carbon tetrachloride, the solution was applied to a column charged with aluminum oxide (Brockmann activity grade II), and the column was eluted with carbon tetrachloride to isolate the dark red zone.

1-[1-(1-Oxo-1H-isoindol-3-yl)nonylidene]-2,3-dihydro-1H-isoindol-3-one (IV) was synthesized from capric acid (**II**). Yield 0.61 g (32%), dark red powder readily soluble in benzene, carbon tetrachloride, and chloroform. Electronic absorption spectrum (CCl_4), λ_{max} , nm (D/D_{max}): 457 (0.87), 427 (1.00). ^1H NMR spectrum, δ , ppm: 10.99 s (1H), 7.84–7.22 m (8H), 2.26 t (2H), 1.25 s (12H), 0.86 t (3H). Mass spectrum (EI), m/z (I_{rel} , %): 386 [M] $^+$ (25), 371 (35), 287 (33), 120 (100). Found, %: C 78.22; H 6.85; N 7.16. $\text{C}_{25}\text{H}_{26}\text{N}_2\text{O}_2$. Calculated, %: C 77.69; H 6.78; N 7.25.

1-[1-(1-Oxo-1H-isoindol-3-yl)heptadecylidene]-2,3-dihydro-1H-isoindol-3-one (V) was synthesized from stearic acid (**III**). Yield 0.76 g (30%), dark red waxy material readily soluble in benzene, carbon tetrachloride, and chloroform. Electronic absorption spectrum (CCl_4), λ_{max} , nm (D/D_{max}): 458 (0.84), 426 (1.00). ^1H NMR spectrum, δ , ppm: 10.92 s (1H), 7.83–7.25 m (8H), 2.21 t (2H), 1.24 s (28H), 0.84 t (3H). Mass spectrum (EI), m/z (I_{rel} , %): 498 [M] $^+$ (29), 368 (38), 331 (32), 160 (100). Found, %: C 79.01; H 8.55; N 6.14. $\text{C}_{33}\text{H}_{42}\text{N}_2\text{O}_2$. Calculated, %: C 79.48; H 8.49; N 6.25.

5,15-Dialkyltetrabenzoporphyrin complexes IX and X (general procedure). a. A mixture of 0.01 mol

of compound **IV** or **V** and 1.0 g of zinc(II) acetate dihydrate was heated to 320°C , kept for 30 min at that temperature, cooled, dissolved in carbon tetrachloride, and applied to a column charged with aluminum oxide (Brockmann activity grade II). The column was eluted with carbon tetrachloride–dioxane (2:1 by volume) to isolate the main green zone.

b. A mixture of 0.02 mol of compound **VIII**, 0.04 mol of acid **II** or **III**, and 0.4 g of zinc(II) oxide was heated to 320°C and kept for 30 min at that temperature. Complexes **IX** and **X** were isolated as described above in a.

(5,15-Dioctyltetrabenzoporphyrinato)zinc(II) (IX). Yield 0.18 g (37%) (a), 0.26 g (34%) (b), dark green powder readily soluble in benzene, chloroform, and carbon tetrachloride and poorly soluble in hexane and acetone. Electronic absorption spectrum (CCl_4), λ_{max} , nm ($\log \epsilon$): 403 (4.58), 427 (5.01), 579 (4.05), 626 (4.51). ^1H NMR spectrum, δ , ppm: 11.03 s (2H), 7.75–7.36 m (16H), 2.77 t (4H), 1.36 s (24H), 0.82 t (6H). Found, %: C 78.41; H 7.15; N 6.84. $\text{C}_{52}\text{H}_{52}\text{N}_4\text{Zn}$. Calculated, %: C 78.23; H 6.56; N 7.02.

(5,15-Dihexadecyltetrabenzoporphyrinato)zinc(II) (X). Yield 0.23 g (37%) (a), 0.28 g (34%) (b), dark green waxy material readily soluble in benzene, chloroform, carbon tetrachloride, and hexane and poorly soluble in acetone. Electronic absorption spectrum (CCl_4), λ_{max} , nm ($\log \epsilon$): 402 (4.59), 427 (5.02), 579 (4.03), 626 (4.50). ^1H NMR spectrum, δ , ppm: 11.12 s (2H), 7.77–7.41 m (16H), 2.75 t (4H), 1.33 s (56H), 0.85 t (6H). Found, %: C 80.22; H 8.76; N 5.12. $\text{C}_{68}\text{H}_{84}\text{N}_4\text{Zn}$. Calculated, %: C 79.85; H 8.28; N 5.48.

5,15-Dialkyltetrabenzoporphyrins XI and XII (general procedure). Complex **IX** or **X**, 0.1 g, was dissolved in 10 ml of 100% sulfuric acid, the solution was kept for 2 h at 20°C and diluted with 30 ml of water, and the precipitate was filtered off, washed on a filter with 50 ml of 20% aqueous ammonia and 100 ml of water, dried, and dissolved in carbon tetrachloride. The solution was applied to a column charged with aluminum oxide (Brockmann activity grade II), and the column was eluted with carbon tetrachloride–dioxane (2:1 by volume) to isolate the green zone.

5,15-Dioctyltetrabenzoporphyrin (XI) was synthesized from complex **IX**. Yield 0.07 g (78%), dark green powder readily soluble in benzene, chloroform, and carbon tetrachloride and poorly soluble in hexane and acetone. Electronic absorption spectrum (CCl_4), λ_{max} , nm ($\log \epsilon$): 418 (4.87), 431 (4.91), 565 (4.14),

601 (4.35), 608 (4.38), 616 (4.35), 663 (4.27). ^1H NMR spectrum, δ , ppm: 11.05 s (2H), 7.76–7.33 m (16H), 2.76 t (4H), 1.32 s (24H), 0.84 t (6H), –2.41 s (2H). Found, %: C 85.22; H 7.35; N 6.70. $\text{C}_{52}\text{H}_{54}\text{N}_4$. Calculated, %: C 84.97; H 7.40; N 7.62.

5,15-Dihexadecyltetrabenzoporphyrin (XII) was synthesized from complex **X**. Yield 0.06 g (67%), dark green powder readily soluble in benzene, chloroform, carbon tetrachloride, and hexane and poorly soluble in acetone. Electronic absorption spectrum (CCl_4), λ_{max} , nm ($\log \epsilon$): 419 (4.86), 433 (4.90), 565 (4.15), 603 (4.35), 608 (4.37), 616 (4.35), 663 (4.28). ^1H NMR spectrum, δ , ppm: 11.05 s (2H), 7.78–7.43 m (16H), 2.72 t (4H), 1.30 s (56H), 0.86 t (6H), –2.35 s (2H). Found, %: C 85.20; H 10.12; N 4.62. $\text{C}_{68}\text{H}_{86}\text{N}_4$. Calculated, %: C 85.13; H 9.03; N 5.84.

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